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Case Report

Small Bowel Metastasis with Multiple Sites of Perforation Caused by Anaplastic Thyroid Carcinoma Metastasis: A Case Report

Nawaphan Taengsakul

Department of Surgery, Princess Srisavangavadhana College of Medicine, Chulabhorn Royal Academy. Bangkok, Thailand

ABSTRACT

Introduction: Anaplastic thyroid carcinoma (ATC) is an extremely aggressive cancer with a very poor prognosis. The lungs, pleura, adrenal glands, and liver are the most common sites of metastasis; metastasis to the digestive tract is rare.

Case Presentation: The patient was a 63-year-old man with ATC was treated with pembrolizumab and lenvatinib. Concomitant venous thromboembolism was being treated with direct oral anticoagulants. He developed peritonitis, and revealed perforation sites associated with an intestinal mass.

Clinical Discussion: ATC with small bowel metastasis is uncommon. However, physicians should be aware of this possibility, especially in patients planned targeted therapy.

Conclusion: Small bowel metastasis of ATC is rare and results in tumor-associated perforation. Small bowel metastasis should be investigated in patients with ATC who present with gastrointestinal hemorrhage. Evidence of small bowel metastasis influences the choice of anticoagulant and systemic cancer treatment in ATC patients.

Keywords: Anaplastic thyroid carcinoma, Small bowel metastasis, Small bowel perforation, Case report

Author conflict of interest: none

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Corresponding Authors: Nawaphan Taengsakul, MD, FRCST.
Department of Surgery, Princess Srisavangavadhana College of Medicine, Chulabhorn Royal Academy. Bangkok, Thailand. 906 Kamphaeng Phet 6 Rd., Talat Bang khen, Lak Si, Bangkok 10210, Thailand.
Tel. +66-2-576-6791 Fax. +66-2-576-6791
E-mail: nawaphan.tan@cra.ac.th

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Introduction

Anaplastic thyroid carcinoma (ATC) is an extremely aggressive cancer with a very poor prognosis[1]. The lungs, pleura, adrenal glands, and liver are the most common sites of metastasis[2]; metastasis to the digestive tract is rare[2]. Herein, we describe a case of ATC treated by total thyroidectomy and targeted therapy. The ATC metastasized to the small bowel, resulting in bowel perforation and peritonitis. This work has been reported in line with the SCARE reporting guidelines[3].

Case Presentation

A 60-year-old man underwent total thyroidectomy at another hospital in January 2023 to treat a thyroid mass. He had no underlying disease and reported no family history of cancer or disease. The pathological report revealed a high-grade epithelioid neoplasm with lympho-vascular and perineural invasion in the right thyroid lobe. The patient was diagnosed with ATC, which local recurrence grew rapidly postoperatively. Neck and chest computed tomography (CT) revealed an ill-defined hypodense lesion on the right side of the thyroid with obliterated the right internal jugular vein and compressed the trachea. Other findings comprised thrombi in the right internal jugular vein and right brachiocephalic vein, which extended to the superior vena cava, as well as multiple pulmonary metastases (Figure 1). The patient was referred to our institution and started treatment with edoxaban 60 mg once daily. Pembrolizumab and lenvatinib were started for ATC treatment.

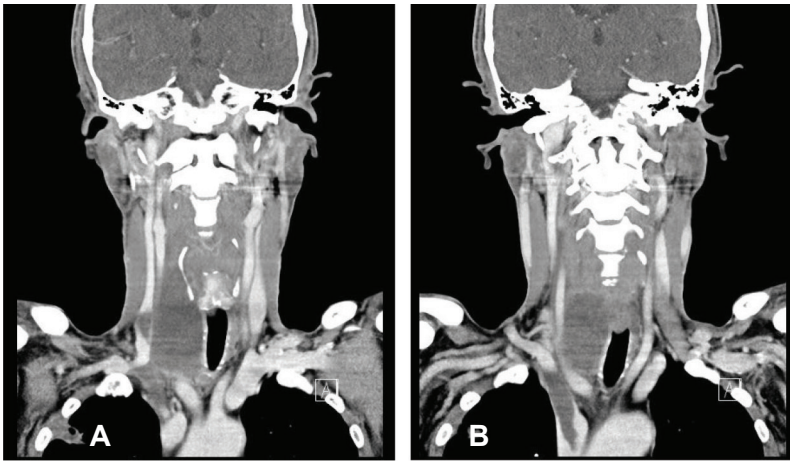


Figure 1 Computed tomography (CT) showing an ill-defined hypodense lesion measuring 3.8 × 3.4 × 7.3 cm in the right thyroid, obliterating the right internal jugular vein. Intraluminal thrombi in the right internal jugular vein (arrow in panel A) and right brachiocephalic vein (arrow in panel B) are also seen.

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In mid-July 2023, he experienced abdominal pain with melena. Gastroscopy and colonoscopy were performed, and no bleeding point was identified. Apixaban 5 mg twice a day was started after endoscopy. Two weeks after the endoscopy, the patient presented to the emergency room with abdominal pain. The patient's pain began as epigastric pain and progressed to lower abdominal pain. The following findings were identified on presentation: body temperature: 36.9°C, pulse rate: 90 beats per minute, respiratory rate: 20 breaths per minute, blood pressure: 122/83 mmHg, oxygen saturation: 98%. Physical examination revealed generalized abdominal tenderness with guarding. An acute abdominal X-ray series revealed small bowel dilatation (Figure 2). Blood laboratory examinations revealed mild leukocytosis $9.7 \times 10^3/\mu L$ (reference: $4–11 \times 10^3/\mu L$) with 88.9% neutrophils predominating (reference: 39.6%–67%). CT revealed a proximal jejunal focal wall defect with a small amount of pneumoperitoneum. There was diffuse bowel wall thickening and liver metastasis was suspected (Figure 3). We then decided to perform emergent exploratory laparotomy after discussing the plan and associated risks with the patient. Preoperatively, 45.45 U/kg of three-factor prothrombin complex concentrate (Profilnine®; Grifols Biologicals, Inc., Los Angeles, CA, USA; 2500 units intravenously) was administrated as a reversal agent. Intraoperatively, we identified three perforation sites, with an ulcerative mass. The perforations were located in the proximal jejunum 30 cm from the duodenojejunal junction, the mid-jejunum, and the ileum (50 cm from the ileocecal valve) (Figure 4). All perforation sites were resected. Multiple ulcerative masses with perforation were observed in the specimen (Figure 4). Histopathological findings revealed four foci of poorly differentiated neoplasia with macroscopic tumor perforation. It was mostly

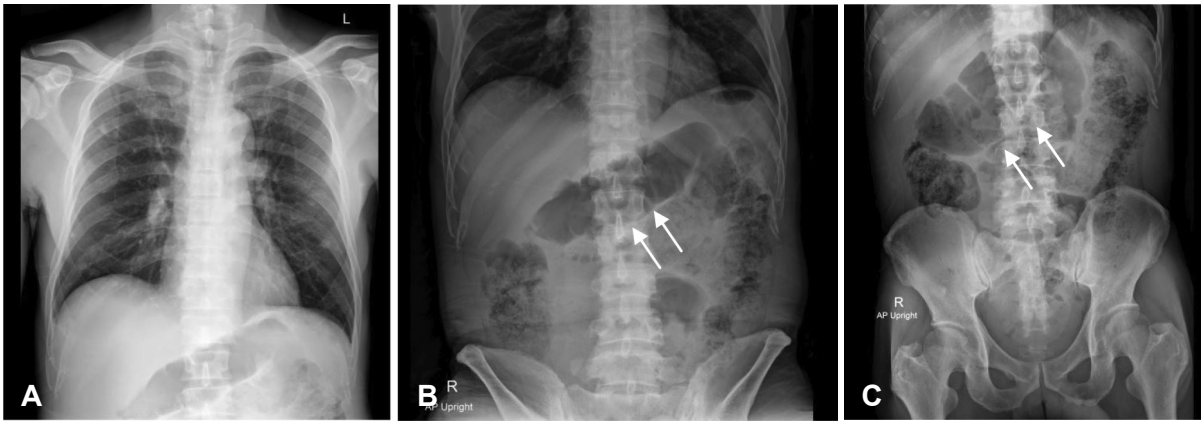


Figure 2 Acute abdominal X-ray series at admission showing segmental small bowel dilatation (arrows) without subdiaphragmatic air.

considered that ATC metastasis had occurred (Figure 5).

Postoperatively, the patient recovered well and was discharged on postoperative day 7. Apixaban was started on postoperative day 2, and there were no postoperative bleeding complications. Although the patient recovered well, he developed anorexia and chronic neck pain after discharge. CT revealed a segmental pulmonary embolism in the right lower branch of the pulmonary artery, as well as several newly hypoenhancing masses throughout the liver. We discussed the prognosis and treatment plan with the patient and his family, who chose primarily supportive treatment and pain control. The patient died 5 weeks after the operation.



Figure 3 Computed tomography (CT) at admission showing a 5-mm focal wall defect in the thickened proximal jejunum (arrow in panel A) with a small amount of pneumoperitoneum (arrow in panel B). Several liver metastases in both the right and left hepatic lobes are visible (arrow in panel C).

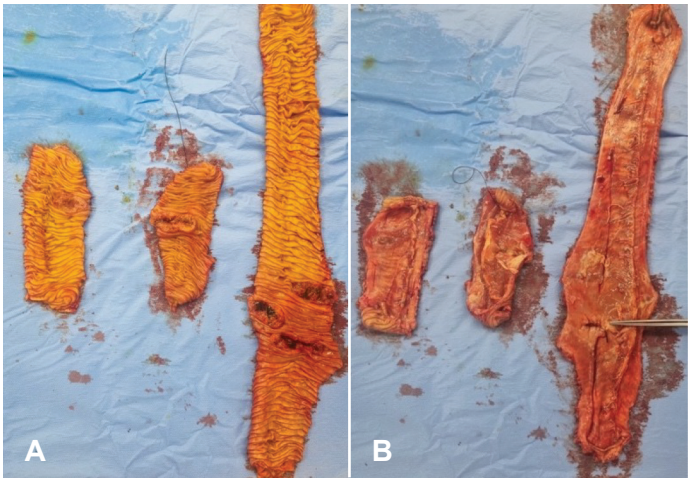


Figure 4 Resected small bowel segment showing multiple sites of perforated ulceration in the intraluminal (A) and extraluminal views (B). The largest perforated site was identified at tip of forceps in the picture.
The small bowel segment specimen shows multiple sites of perforated ulceration in both intraluminal (figure 4A) and extraluminal views (figure 4B).

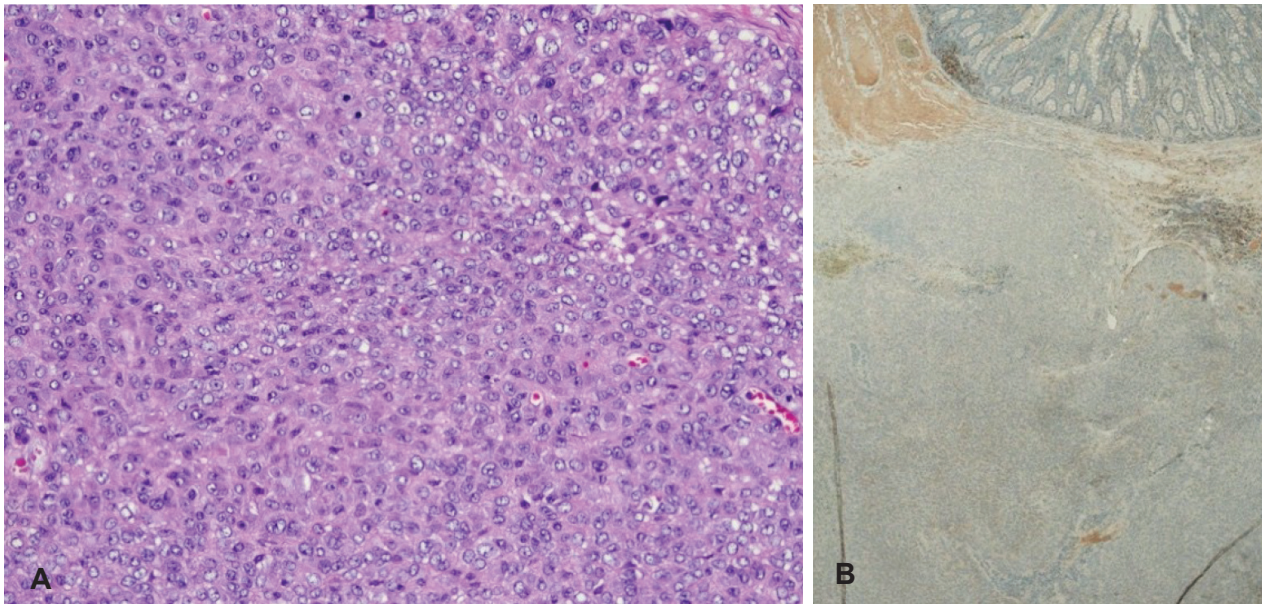


Figure 5 Histopathological images of the perforating small bowel mass showing neoplastic cells with enlarged, marked, pleomorphic nuclei and abundant cytoplasm. Mitotic figures are frequent (A). Immunohistochemical staining for PAX-8 was negative (B).

Discussion

ATC is a rapidly growing carcinoma associated with a poor prognosis and mean survival time of 5-6 months[1]. Approximately 20%–50% of patients have distant metastasis when diagnosed and 90% have adjacent organ invasion[4]. Besic et al.[3] analyzed 205 patients with ATC and found the most common sites of metastasis were the lung (78%), intrathoracic lymph nodes (58%), cervical lymph nodes (51%), pleura (29%), adrenal glands (24%), liver (20%), brain (18%), heart (18%), and retroperitoneal lymph nodes (18%); only one case of small bowel metastasis was identified[3]. Additionally, only eight reported cases of small intestinal metastasis of ATC were identified[5–11], indicating that ATC with small bowel metastasis is rare. Furthermore, the three clinical presentations of small bowel metastasis of ATC comprised tumor perforation (four cases)[6,9–11], intussusception (two cases), and persistent abdominal discomfort (one case)[5]. One study reported small bowel metastasis identified in autopsy results[3]. Table 1 shows the characteristics of all reported cases.

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Table 1 Literature review of case reports showing the first author's name, year of publication, patient's characteristics, treatment, prognosis, and cause of death.

Case	Author	Year	Age	Gender	Chief complaint	Examination	Complications associated with the Metastatic	Metastatic site	Treatment	Prognosis	Cause of death
1	Phillips[5]	1987	66	F	Abdominal pain	Enteroclysis	Bleeding	Jejunum	Open surgery	2 months	Unknown
2	Kim[6]	1994	66	M	Abdominal pain	-	Perforation	Small bowel	Open surgery	Unknown	Unknown
3	Ricciardelli[7]	2006	68	F	Abdominal pain	CT	Intussusception	Brain, lung, ileum	Open surgery	2 months	Respiratory insufficiency
4	Yazaki[8]	2011	41	M	Abdominal pain	U/S, CT	Bleeding, intussusception	Lung, liver, jejunum, ileum	Laparoscopic surgery	20 days	DIC
5	Kobayashi[9]	2015	68	M	Abdominal pain with fever	CT	Perforation	Esophagus, jejunum	Open surgery	8 months	Tracheal stenosis
6	Gavriilidou[10]	2019	57	F	Abdominal pain	CT	Perforation	Lung, brain, small intestine	Open surgery	26 days	Cancer
7	Hrudka[11]	2021	66	F	Abdominal pain with fever	CT	Perforation	Small intestine	No operation	0 months	Cardiac arrest due to sepsis
8	Our case	2023	60	M	Abdominal pain	CT	Perforation	Lung, liver, small intestine	Open surgery	5 weeks	Cancer

M, male; F, female; U/S, ultrasonography; CT, computed tomography; DIC, disseminated intravascular coagulation



In our case, he presented with gastrointestinal hemorrhage and developed tumor perforation. The primary learning point in this case is to look for small bowel metastases in patients with ATC who present with gastrointestinal hemorrhage. Abdominal and pelvic CT should have been performed.

The diagnosis of ATC is based on the clinical presentation of an older patient with a large, symptomatic, rapidly growing mass, and pathological assessment reveals a highly invasive tumor, characterized by high cellular proliferation with atypical mitoses[1]. Despite the fact that the immunohistochemical staining results in our case are atypical, the history and microscopic findings indicate that the metastatic tumors most likely originated from ATC.

Pembrolizumab is an immunotherapeutic that has been used in patients with ATC[12]. Lenvatinib is a potent angiogenic drug with a multikinase inhibitor mechanism approved for ATC treatment[12]. Adverse events, such as bleeding, fistula formation and small bowel perforation especially in patients with bowel metastasis were reported[12].

In cases of thyroid cancer, numerous factors contribute to thrombosis, including venous compression, vascular invasion, venous injury or ligation during surgery, and a prothrombotic state[13]. Furthermore, levothyroxine therapy may have a prothrombotic effect, and tyrosine kinase inhibitors have also been associated with VTE[13]. In our case, right internal jugular vein compression was identified as a risk factor. Additionally, the use of levothyroxine and sorafenib increased the risk of VTE. With respect to VTE treatment, edoxaban has been recommended for cancer patients with VTE and a low risk of bleeding[14]. Apixaban had the lowest degree of major gastrointestinal risk compared with other direct oral anticoagulants[15].

Conclusion

Small bowel metastasis of ATC is rare and results in tumor bleeding and perforation, which increases morbidity and mortality. Patients with ATC who present with gastrointestinal hemorrhage should be evaluated for small bowel metastasis. Evidence of small bowel metastasis influences the choice of both VTE and systemic cancer treatments in ATC patients.

Ethical Approval and Compliance with the Tenets of the Declaration of Helsinki

This study was exempted from the need to obtain ethical approval by the Ethics Committee of Human Research of our Institution. The project number is EC 109/2566, which was provided as approval by the committee to report the case.

Provenance and peer review

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not-for-profit sectors.

Registration of research studies

Not applicable. This is a case report and not a research study.

Consent for publication

Written informed consent was obtained from the patient for publication and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Authors' contributions

Nawaphan Taengsakul: Conceptualization, investigation, methodology, and drafting, editing, revising, and reviewing the manuscript.

Guarantor

Nawaphan Taengsakul is the person in charge of the publication of this manuscript.

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